08/982,965

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/982,965	12/02/97	LOWELL G	35929200110

EXAMINER	
BUEVENS, P	
ART UNIT	**PAPER NUMBER**
1648	2

HM21/0826

JOHN F MORAN
OFFICE OF COMMAND JUDGE ADVOCATE
HQ USAMRDC DEPT OF THE ARMY
FORT DETRICK
FREDERICK MD 21702-5012

DATE MAILED: 08/26/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-4 is/are pending in the application.
☐ Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-4 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

✓ ☒ Notice to Comply with Sequence Rules
✓ ☒ Notice of Reference Cited, PTO-892 2 pages
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

The Art Unit location of your application in the Patent and Trademark Office has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648.

The status of the related application(s) cited at the first page of the specification should be updated, if necessary, to ensure a properly completed file record. It is noted that the filing papers of the instant application indicated that this application is a divisional of application Serial No. 08/143,365, now U.S. Patent No. 5,726,292. However, there is no indication of related application(s) at the first line of the specification. It is noted that 08/143,365 is itself a continuation-in-part of several other applications and it is unclear if applicant is intending to claim priority to the earlier filed applications. Further, Applicant is required to file a request for correction of the filing receipt since the file wrapper does not properly refer to the parent applications.

Applicant is encouraged to file an information disclosure statement including (1) a form PTO-1449, "Information Disclosure Citation" listing patents, publications and other information material to the instant application; (2) a concise explanation of the relevance of each listed item; (3) a copy of each listed item; and (4) a disclosure of related co-pending applications. See 37 C.F.R. §§ 1.97-1.98.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 for the reason(s) set forth on the attached Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence

Disclosures.

APPLICANT IS GIVEN THREE MONTHS (THE SHORTENED STATUTORY TIME PERIOD FOR RESPONSE TO THIS OFFICE ACTION) FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R. § 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Applicant is required to submit a substitute specification. A substitute specification is required because the specification has been filed with numerous notations corresponding to amendments and/or corrections to both the specification and claims made in an earlier filed application. These corrections are not properly submitted in a preliminary amendment in the instant application nor have they been properly initialed. The substitute specification filed must be accompanied by a statement that it contains no new matter. Such statement must be a verified statement if made by a person not registered to practice before the Office.

This application does not contain an Abstract of the Disclosure as required by 37 C.F.R. 1.72(b). An Abstract on a separate sheet is required.

The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. 602.1 and 602.02. The oath or declaration is defective because:

(1). It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. § 120 which

discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose material information as defined in 37 C.F.R. 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

(2). Applicant has not given a post office address anywhere in the application papers as required by 37 C.F.R. 1.33(a). A statement over Applicant's signature providing a complete post office address is required. Further, Applicant's residence address is illegible.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The constructs and compositions of claims 1-4 are directed to vaccines for HIV comprising HIV-1 gp160 envelope protein and a proteosome (see page 2, lines 18-25 and claim 2). However, Applicant's specification does not set forth sufficient convincing evidence to establish that one skilled in the art could use the constructs and compositions as claimed with a reasonable expectation of success and without undue

experimentation. It is well known in the art that retroviral infections in general, and HIV infections in particular, are refractory to anti-viral therapies. The obstacles to therapy of HIV are well documented in the literature. These obstacles include: 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein; 2) the fact that the modes of viral transmission include both virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission; 3) the existence of a latent form of the virus; 4) the ability of the virus to evade immune responses in the central nervous system due to the blood-brain barrier; and 5) the complexity and variation of the pathology of HIV infection in different individuals. The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed invention with a reasonable expectation of success and without undue experimentation.

Further, it is well known in the art that individuals infected with HIV produce neutralizing antibodies to the virus, yet these antibodies are not protective and do not prevent the infection from progressing to its lethal conclusion. Further, as taught by Fahey et al. (R), clinical trials using a variety of immunologically based therapies have not yielded successful results in the treatment and/or prevention of HIV infection (see Table 1).. Fahey et al. particularly discloses that monoclonal antibody therapies have not provided any clinical benefits and "it is not clear how adding these additional antibodies would make a difference" (see page 3, second column, third full paragraph). The failure of all immune-system-boosting therapies for treating AIDS is further discussed by Fox (S). The teachings of Fahey et al. and Fox are further confirmed by Haynes et al. (T). Haynes et al. teach the major scientific obstacles blocking development of HIV vaccines

(see page 40, first column, second full paragraph). Further, Haynes et al. teach that "Current animal models of either HIV or simian immunodeficiency virus (SIV) fall short of precisely mirroring human HIV infection" and that "lacking these models, researchers must turn towards human clinical trials to answer many of the difficult questions about HIV pathogenesis and HIV vaccine development" (see page 40, first column, third full paragraph). Thus, it is clear from the evidence of Fahey et al., Fox, and Haynes et al. that the ability to treat and/or prevent HIV infection is highly unpredictable and has met with very little success.

Applicants have not provided any convincing evidence that their claimed invention is indeed useful as a therapeutic or preventative for HIV infection and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> **A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**
>
> **Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an**

obligation of assignment to the same person.

Claims 1-4 are rejected under 35 U.S.C. § 103 as being unpatentable over Lowell et al. (U) or Lowell et al. (V) or Smith et al. (W) or Avraham et al. (X) in view of Ratner et al. (Y). Lowell et al. (U), Lowell et al. (V) and Smith et al. (W) all disclose the production of proteosome compositions suitable for use as vaccines. The compositions comprise a antigenic protein region, a hydrophobic anchor and a proteosome (see Abstracts of each reference, for example). These compositions appear identical in composition and methods of making as those of the claimed invention. Avraham et al. teach the production of proteosome vaccines comprising the V3 loop peptide of gp160. Avraham further disclose the use of a lauroyl or hydrophobic peptide prefix for use in constructing the proteosome vaccines. Thus, the teachings of any of Lowell et al. (U) or Lowell et al. (V) or Smith et al. (W) or Avraham et al. (X) establish that those of ordinary skill in the art had knowledge of the production of proteosomes and their use in production of vaccines and Avraham et al. establish that those of ordinary skill in the art recognized the use of proteosomes with HIV antigens for the production of vaccines against HIV. The prior art references do not disclose the use of intact gp160.

However, Ratner et al. disclose the complete genome of HIV (HTLV-III) including the sequence of gp160 and indicates that the envelope sequence corresponds to the envelope protein of HIV (see page 282, first column, fifth full paragraph). Further, it is well known in the viral art that envelope proteins of enveloped viruses are highly antigenic and often used as vaccine targets. Thus, absent convincing objective evidence to the contrary, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the proteosomes of any of Lowell et al. (U) or Lowell et al. (V) or Smith et al. (W) or Avraham et al. (X) and to substitute the gp160 envelope protein of

HIV as the antigen of choice for the expected benefit of obtaining an improved therapeutic reagent for treating/preventing HIV infection. One of ordinary skill in the art would have been motivated by the long felt need for improved HIV therapeutics and would have had a reasonable expectation of success since Avraham et al. had produced proteosomes using V3 peptides obtained from gp160.

No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. The Fax number is (703) 308-4242. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Robert D. Budens at (703) 308-2960. The Examiner can normally be reached Monday-Thursday from 6:30 AM-4:00 PM, (EST). The Examiner can also be reached on alternate Fridays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Don Adams, can be reached at (703) 308-0570.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at (703) 308-0196.

Robert D. Budens
Primary Examiner
Art Unit 1648

rdb
August 17, 1998